INVASIVE MENINGOCOCCAL DISEASE

Neisseria meningitidis

REPORT IMMEDIATELY

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

There are different clinical manifestations of *N. meningitidis*:

Bacteremia without sepsis:

- This tends to be a mild disease, often appearing as a upper respiratory disease or viral exantham (rash). Blood cultures will be positive for *N. meningitidis.* This disease has a chronic state that can be mistaken for gonococcemia. Chronic bacteremia may be due to an immunologic deficiency.

Meningococcemia without meningitis:

- The patient appears septic, with leukocytosis (increased white blood cells), skin rash, generalized malaise, weakness, headache, and hypotension. Petechiae and disseminated intravascular coagulation (DIC) are also common. Meningococcemia is the most severe presentation of this disease.

Meningitis with or without meningococcemia:

- Patients present with headache, fever, and meningeal signs, along with a cloudy CSF. The presentation varies and patients may not have the above symptoms.

Meningoencephalitis manifestations:

- Patients are profoundly ill with meningeal signs and septic spinal fluid. Deep tendon and superficial reflexes are altered (absent or hyperactive). Pathologic reflexes are frequently present.

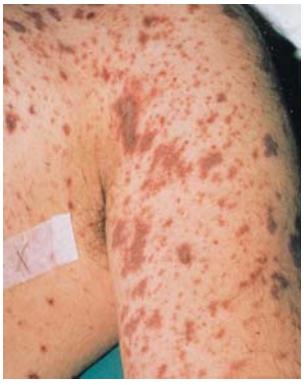
Pneumonia:

- Symptoms include cough, chest pain, chills, rales, and pharyngitis. This can be difficult to diagnose because a sputum culture could be contaminated with respiratory flora (from a carrier), and the incidence of sepsis is low (therefore blood cultures are unlikely to be of value).

Other manifestations include:

- Epiglottitis
- Urethritis
- Arthritis
- Pericarditis

Patients can progress between manifestations during their course of illness.



Petechial lesions are common with this disease, but can be missed. Lesions can occur in obscure places such as the hard palate and conjunctiva, but is generally seen on the trunk and lower limbs. It is important to carefully examine the patient, as petechia can sometimes be found only in pressure points, such as under socks or underwear elastic. The petechia rash corresponds to thrombocytopenia and is an indicator of

disseminated intravascular coagulopathy (DIC). Some patients may also present with a maculopapular rash, but it is transient.

Causative Agent:

Meningococcal meningitis is caused by Gram-negative diplococci, *Neisseria meningitidis*. The sides are flattened and this organism is recognizable in Gram stain by an experienced microscopist. There is a polysaccharide capsule surrounding the organism; differences in this capsule are the basis for the serogroup. This organism is fastidious in its growth requirements, but virtually all clinical microbiology laboratories can grow it in culture.

There are at least 13 serogroups of this organism: A, B, C, D, X, Y, Z, E, W-135, H, I, K, and L. In the U.S., serogroups B and Y each cause approximately 35% of invasive meningococcal disease. Serogroup C causes approximately 24% with W-135 causing 2%. Recently, Utah has seen a decrease in invasive meningococcal disease due to serogroup B.

Differential Diagnosis:

Neisseria meningitidis is an invasive bacterial disease and must be differentiated from bacteria that create similar symptoms, such as Streptococcus pneumoniae, Group A and B strep, and Haemophilus influenzae. Neisseria have a characteristic presence on Gram stain (Gram-negative diplococci) which can assist with discrimination, especially when antibiotics have been started prior to collection of specimens for bacterial culture.

Laboratory identification:

N. meningitidis is not difficult to identify in the laboratory. Typical specimens to obtain include blood, CSF, or synovial, pleural, or pericardial fluid.

- **Culture –** Typically, meningococcal meningitis is identified via Gram stain of the CSF and subsequent culture. The morphology of the organism is sufficient to suspect meningococcal meningitis rapidly through the Gram stain. The confirmatory culture should be available the next day. One problem with culture is with patients who are treated with antibiotics PRIOR to the spinal tap. Ideally, both CSF and blood cultures should be collected before initiating antibiotic therapy. When this is not possible, both blood and CSF culture should be collected as soon as possible after the initiation of antimicrobial therapy. Cultures can be rendered sterile as soon as 2 hours after initiation of antimicrobial therapy.
- **PCR amplification (DNA detection) –** PCR amplification has the advantage of being rapid, and being less susceptible to prior antibiotic treatment than culture. PCR is highly sensitive and specific. Unfortunately, this test is not widely available.
- **Latex agglutination** – This is now rarely performed. The Gram stain is generally thought to be a preferable rapid test in CSF.

Treatment:
Clinicians should consult with an infectious disease specialist or appropriate references for current therapies.

Drugs that are not effective include first-generation cephalosporins and sulfonamides.

Case fatality:
The case fatality is highly variable and depends upon the disease and availability of appropriate health care. Meningitis or pneumonia fatality is about 7-13%, whereas fatality with septicemia can be as high as 19%. Some survivors (~10-20%) will suffer from long-term sequelae such as hearing loss, mental deficits, and loss of limbs.

Reservoir:
Humans. Up to 25% of the population carry *N. meningitidis* in their nasal mucosa without symptoms. In closed populations, such as military or residential living centers, carriage rates can be much higher. Carriage can be infrequent, intermittent, or long-lasting.

Transmission:
Carriers spread the organism via the respiratory route. Transmission is relatively inefficient, and close contact is necessary.

Susceptibility:
Disease rates are high in infancy (3-5 month olds), and then decrease from adolescence through young adulthood, and rise after the age of 60 years.

Between 1991 and 1998, the rate of meningococcal disease in people aged 18-23 years has been higher than for the general population.

Individuals thought to be at higher risk include those with underlying immune deficiencies (asplenia, complement deficiency). Other risk factors include crowding, low socioeconomic status, tobacco smoke, and a concurrent respiratory tract infection. Outbreaks typically occur in closed settings such as childcare, schools and colleges (especially freshmen living in dormatories), and military training camps.

Household contacts are at increased risk (from 500 to 4,000 fold higher than non-household contacts) of developing disease following exposure.

Incubation period:
The incubation period is usually 3-4 days, with a range of 1-10 days.

Period of communicability:
People are thought to be infectious until 24 hours after initiation of antibiotic therapy.

Epidemiology:

The epidemiology of meningococcal meningitis is still unclear. Various questions remain unanswered on the sporadic, episodic nature of this disease, the susceptibility of certain populations, carrier eradication, transmission, and the failure to produce a serogroup B vaccine that elicits immunity. *N. meningitidis* is the second most common cause of community-acquired adult bacterial meningitis (and the leading cause in children and young adults since the availability of the HIB vaccine). People may be more likely to acquire *N. meningitidis* with a co-morbidity of a viral infection.

- Carrier state – One of the unusual features of *N. meningitidis* is that it can be carried in the throats of perfectly healthy individuals. However, there is a positive relationship between the rate of carriage (or possibly transmission, not carriage) in a population, and the onset, rise, and decline of an epidemic. Other respiratory diseases usually cause no change or a decrease in the carriage rate of *N. meningitidis*.

  Carriers fall into three groups – chronic, intermittent, and transient. Chronic carriers can be colonized for up to 2 years. The carrier state appears to immunize the carrier.

- Invasive disease – There is a correlation between the capsular phase variation, bacterial invasion, and disease outbreaks. People with invasive disease are more likely to have been recently colonized; disease is thought to occur within the first week of acquisition.

- Outbreaks - Shifts in the age distribution can forecast the onset of an epidemic situation. Epidemics tend to occur in 5-19 year olds. Less than 5% of meningococcal meningitis cases are due to outbreaks. Outbreaks are most likely to occur in childcare settings, military recruit camps, schools, and colleges.

The current rate of disease in the U.S. is 1.3 cases/100,000 population (per year). In the U.S., serogroups C and Y are the most prevalent, each causing approximately 33% of the reported invasive disease. There is some seasonality associated with this disease – it is most common in winter and spring. Recent Utah data shows a gradual shift over the past 5 years away from serogroup B and towards serogroup Y.

Epidemic potential is related to serogroup. Epidemics are most likely among the poorest socioeconomic groups, with crowding and lack of sanitation common.

Typical Causes of Epidemic Invasive Disease (Worldwide)		
Serogroup	**Where**	**Attack Rate**
A	Less developed countries	Up to 500 cases per 100,000 population
B	Developed countries	50-100 case per 100,000 population
C	Developed and undeveloped countries	Up to 500 cases per 100,000 population

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

Public health has the primary responsibility for identifying and chemoprophylaxing contacts to identified cases. Other important public health responsibilities include:

- Investigating cases to determine possible linkage to other cases in Utah or beyond.
- Collecting demographic information to identify "at risk" populations.
- Encouraging "at risk" populations to receive immunization.
- Monitoring levels of disease in the community.
- Analyzing disease trends.
- Tracking age distribution and types of invasive meningococcal disease reported to public health, to determine whether a transition from a non-epidemic to an epidemic period is occurring. (Remember that epidemic periods predominantly affect those in the 5-19 year age range.)
- Monitor reported serogroups, and collecting and reporting sufficient information to determine whether there is a changing pattern and whether vaccine is covering the majority of reported cases.

Prevention:

There is a vaccine available for some serotypes of meningococcal meningitis. The immunogenicity of serogroups A, C, Y, and W-135 are good, but B doesn't stimulate an immune response. This is thought to be due to the size of the B antigen.

Routine vaccination with Menomune vaccine (Menomune® by Connaught Laboratories, Inc.) is not recommended, due to ineffectiveness in children under 2 as well as the short duration of immunity.

A new version of the *N. meningitidis* vaccine (Menactra® by Sanofi Pasteur) has been licensed for individuals between 11 and 55 years of age. This new vaccine is effective against serogroups A, C, Y, and W-135, but the immunogenicity of the vaccine is enhanced through conjugation, so the immunity is thought to be higher and longer lasting.

Chemoprophylaxis:

If the patient has a positive culture for *Neisseria meningitidis*, then all close contacts should be prophylaxed with antibiotics. If the patient was treated with antibiotics before the culture was obtained, and no bacteria are found, then the decision to prophylax close contacts becomes more difficult. Each situation should be reviewed individually to determine the likelihood of invasive meningococcal disease. The State Epidemiologist can assist with this review process.

- **Antibiotics** - Prophylaxis typically consists of
  - Rifampin

- Adults: 600 mg q 12h for 2 days;
- Children <1 month, 5 mg/kg q12h for 2 days;
- Children >1 month, 10 mg/kg q12h <maximum 600 mg/day> orally for 2 days);
- Resistance is known to occur during prophylaxis with rifampin.

o Ciprofloxacin
- Adults: 500 mg single dose, or

o Ceftriaxone
- Adults 250 mg single IM dose;
- Children <15 years, 125 mg, single IM dose).

Note: rifampin and ciprofloxacin are not recommended for pregnant or possibly pregnant women.

Penicillin and sulfonamides are not appropriate drugs for prophylaxis.

Vaccine:

Widespread vaccination of contacts would not be advised except during outbreaks. Ensure that the vaccine covers the serogroup of the circulating bacteria before implementing this strategy in an outbreak setting.

Isolation and quarantine requirements:

Isolation: Patients should be on respiratory isolation until 24 hours after starting antibiotic therapy.
Hospital: Patients should be on respiratory isolation until 24 hours after starting antibiotic therapy.
Quarantine: Not applicable.

✓CASE INVESTIGATION

Reporting:

All cases of invasive meningococcal disease are immediately reportable in Utah. This disease should be reported when suspected, not just when confirmed.

Case definition:

Meningococcal Disease (2005):

Clinical Description

Meningococcal disease manifests most commonly as meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock, and death. However, other manifestations might be observed.

Case Classification

Confirmed:

o A clinically compatible case AND isolation of Neisseria meningitidis from a normally sterile site (e.g., blood or cerebrospinal fluid {CSF} or, less

commonly, synovial, pleural, or pericardial fluid) or skin scrapings of purpuric lesions.

Probable:

- A clinically compatible case that has either:
  - Evidence of N. meningitidis DNA using a validated polymerase chain reaction (PCR), obtained from a normally sterile site (e.g., blood or CSF),

    OR
  - Evidence of N. meningitidis antigen by immunohistochemistry (IHC) on formaline-fixed tissue or latex agglutination of CSF.

Suspect:

- Clinical purpura fulminans in the absence of a positive blood culture
- A clinically compatible case with gram negative diplococci from a normally sterile site (e.g., blood or CSF).

Case Investigation Process:

- Confirm the diagnosis (if patient does not have a confirmed diagnosis, but the clinician determines that the disease was likely to be due to bacterial meningitis, then it may be prudent to continue with chemoprophylaxis).
- Determine who is at risk. People thought to be at highest risk include household, childcare, and nursery school contacts. In addition, close contacts include people who have had contact with the patient's oral secretions, such as kissing, sharing toothbrushes, sharing utensils, sharing food (food that might have oral secretions, not just eating at the same table), and people who frequently ate or slept in the same dwelling as the patient. The patient is infectious during the following period of time:
  - From 7 days before the onset of their disease UNTIL
  - Successful completion of 24 hours of antibiotics.
- You should identify all close contacts to the patient that occurred during the above risk period.
- Notify UDOH.
- Ensure that contacts are offered prophylaxis:
  - Ideally, this should occur within 24 hours after the case is identified.
  - Prophylaxis given more than 14 days after the onset of illness in the index case is of limited or no value.
- All close contacts should be observed for 10 days following exposure. If any febrile illness develops, contacts should receive immediate medical attention.
- For patients on airline flights lasting more than 8 hours, passengers sitting directly next to the patient are candidates for prophylaxis.
- Health care workers are low risk UNLESS they provided mouth-to-mouth resuscitation or unprotected contact during endotracheal intubation during 7 days prior to onset of disease OR after disease onset, but before 24 hours of antimicrobial therapy has been completed.

- Consider starting enhanced surveillance for additional cases of illness.
- Ensure that the organism is serogrouped.
- Fill out the current Active Bacterial Core Surveillance Case Report Form (2002) and fax the completed form to the Utah Department of Health.
- If more than one case is found:
    - Notify the UDOH bacterial disease epidemiologist and request assistance if needed.
    - Investigate for possible links between cases
    - Determine if the outbreak is limited to an organization (e.g. child care, school) or is community-wide.
    - Determine the target group for vaccination.
    - Consider enhanced surveillance or special case-finding methods.
- Ensure that information essential to trend analysis is completely filled out before the investigation is closed. Examples of such information would be: onset date, was patient hospitalized, how long was patient hospitalized, did patient die, etc.

Outbreaks:

An outbreak will be defined as:

- More than two cases in a closed population in a 30 day period;
- Two or more cases with direct epidemiological linkage; or
- More than two cases of PFGE-identical isolates in a 30 day period.

Identification of case contacts:

Case contacts are those that:

- Live in the same household (especially young children).
- Share the same sleeping space (such as military barracks or dorm rooms) during 7 days prior to illness onset.
- Are contacts at day care or nursery during 7 days prior to illness onset.
- Are close social contacts (through kissing, sharing water bottles, cutlery, or very close friends).
- Are medical personnel, if they had unprotected exposure to patient secretions (e.g. mouth to mouth resuscitation, endotracheal intubation, endotracheal tube management) during 7 days prior to illness onset OR after illness onset but before patient has received 24 hours of appropriate antibiotic therapy.

Case contact management:

People who meet the criteria for case contacts should have:

- Prophylactic antibiotics.
    - Throat or nasopharyngeal cultures are of no value in determining who should receive prophylaxis.
- Be under fever surveillance.
    - Initiate appropriate antibiotic therapy for individuals with preliminary signs of disease.

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